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| 09/500,376 | 02/08/2000 | Sandra P. Chang | A-67984/RFT/DSS | 2515 |

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| EXAMINER | |
|---|---|
| NAVARRO, ALBERT MARK | |
| ART UNIT | PAPER NUMBER |
| 1645 | 22 |

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/500,376 | Applicant(s) Chang et al |
|---|---|---|
| | Examiner Mark Navarro | Art Unit 1645 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☐ Responsive to communication(s) filed on _____.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *37-55* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *37-55* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

Applicant's amendment filed March 21, 2003 (Paper Number 21) has been received and entered. Consequently claims 37-55 remain pending in the instant application.

### *Claim Rejections - 35 USC § 112*

1. The rejection of claims 37-55 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. This is a written description rejection.

Applicants are asserting that the claims have been amended to recite that the p42 polypeptide comprises at least a portion of the 42 kDa C-terminal processing fragment of the major merozoite surface protein gp195 from a *Plasmodium falciparum* isolate, and which shares at least one antigenic epitope with a polypeptide according to any one of SEQ ID NO: 2-5. Applicants further assert that the specification discloses a representative number of species of such p42 polypeptides, including FUP, MAD, WEL and K1. Applicants further assert that it is clear from Figure 6 that the corresponding amino acid sequences of the p42 polypeptides are readily determined by aligning the C-terminal sequences of the various gp195 isolates in a manner that maximizes the sequence identity between them. Applicants finally assert that the specification sets forth that the anti-BVp42 antibodies were additionally demonstrated to strongly or

completely inhibit in vivo growth of heterologous and homologous parasites in a well-established primate model.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants are asserting that the claims have been amended to recite that the p42 polypeptide comprises at least a portion of the 42 kDa C-terminal processing fragment of the major merozoite surface protein gp195 from a *Plasmodium falciparum* isolate, and which shares at least one antigenic epitope with a polypeptide according to any one of SEQ ID NO: 2-5. However, even this claim language allows for numerous structural variants, given that a single epitope can comprise as little as 4-5 consecutive amino acids. Applicants are again directed to the Written Description guidelines, specifically Example 13 which deals with protein variants. This is directly analogous to what Applicants are attempting to claim, any polypeptide that happens to share 4-5 consecutive amino acids in common with SEQ ID NO: 2-5, based upon the disclosure of a single p42 polypeptide. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. It is further noted that Applicants assert that the members of the genus all share "functional characteristics" especially when combined with an adjuvant selected from QS-21 and ISA-51. The p42 polypeptides each elicit antibodies that are functionally effective against various Plasmodium falciparum isolates. However, Applicants "function" is not one which identifies members of the genus. Every polypeptide under the correct conditions is

capable of eliciting an immune response. Thus, Applicants have not identified a "function" which identifies members of the genus.

Second, Applicants further assert that the specification discloses a representative number of species of such p42 polypeptides, including FUP, MAD, WEL and K1 and that it is clear from Figure 6 that the corresponding amino acid sequences of the p42 polypeptides are readily determined by aligning the C-terminal sequences of the various gp195 isolates in a manner that maximizes the sequence identity between them. However, while Applicants have shown a working example of a specific p42 protein, this is simply not commensurate in scope with the instantly filed claims directed to any polypeptide sharing as little as an "epitope" in common. Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity or immunogenicity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of "aligning for maximal sequence similarity" results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support

regarding enablement. For instance, sickle cell sickle cell anemia involves a single amino acid substitution of valine for glutamate.

Applicants finally assert that the specification sets forth that the anti-BVp42 antibodies were additionally demonstrated to strongly or completely inhibit in vivo growth of heterologous and homologous parasites in a well-established primate model. However, the particular protein identified in the Examples is not being questioned. Once again, Applicants claims are simply not commensurate in scope with Applicants cited Examples: The claims encompass protein variants having as little as a single epitope (4-5 amino acids) in common with the disclosed protein. As set forth above, the claims encompass numerous structural variants, and it is these variants which do not meet the Written Description guidelines.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 2, 3, 4 and 5 alone are insufficient to describe the genus. Thus, Applicant's have not described a function which is shared by SEQ ID NO: 2, 3, 4, and 5 which would adequately describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to

provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. It is further noted that SEQ ID NO: 2, 3, 4 and 5 are not full length proteins. Given that the function of the non-full length protein is not set forth, the written description of the instant application is supportive of only an antigenic peptide consisting of SEQ ID NO: 2, 3, 4 and 5, since additional amino acids on the N-terminus or C-terminus will have a profound impact on the activity of the protein.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

For reasons of record in Paper Number 17, as well as the reasons set forth above, this rejection is maintained.

2. The rejection of claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the recitation of "substantially reduces" is withdrawn in view of Applicants amendment.

*Claim Rejections - 35 USC § 102*

3. The rejection of claims 37-47, 50 and 53-55 under 35 U.S.C. 102(e) as being anticipated by Speaker et al is withdrawn in view of Applicants amendment.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached

on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

June 11, 2003